

Malatyl Polysaccharides, Their Production and Their Use

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The invention relates to malatyl polysaccharides made of polysaccharides and cis-epoxy succinate or other epoxy carboxylic acids, methods for their production as well as their use in detergents, thickening agents, complexing agents for cations or organic compounds or as ion exchangers for aqueous system or as adjuvants in pharmaceutical applications (for example, tablet bursting agents, suspension stabilizes etc.) or as ingredients in hygiene articles and medical fields.

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In general, reactions of starch or cellulose with epoxides (oxiranes), for example, with ethylene oxide or propylene oxide, to form hydroxyalkyl derivatives have been known for quite some time and have been described in many publications (for example, K. Engelskirchen in "Methoden der organischen Chemie", Vol. E20, p. 2135ff, 1987). Hydroxyalkyl starches or hydroxyalkyl cellulose compounds are non-ionic derivatives which are used often in electrolyte-rich systems, for example, as thickening agents because they react substantially inert in aqueous systems (for example, without viscosity loss) in regard to electrolytes (salts).

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Reactions of starch or cellulose to ionic derivatives have also been described often (see, inter alia, R. L. Davidson, Handbook of Water-soluble Gums and Resins, Chapter 22, 1980). The ionic derivatives have the advantage that they are soluble in cold water and thus cover a large range of applications. Carboxymethyl derivatives (for example, carboxymethyl starch or carboxymethyl cellulose) and oxidized polysaccharides are the best known representatives of ionic derivatives. These derivatives have only one ionic group (carboxyl group) per substituent and are not suitable in an advantageous manner, for example, as co-builders in detergents or water softening agents. In addition, esters of adipic acid (adipate), succinic acid (succinate) or maleic acid are common which result from esterification of the dicarboxylic acid with the glucose of the starch or cellulose. However, in this

reaction one of the functional groups of the two carboxylic groups is lost. This is of great disadvantage when this derivative is to be used as a complexing agent for polyvalent ions (for example, calcium). For example, this complexing property would be advantageous in regard to water softening agents.

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A derivative produced from maleic acid anhydride and starch (or cellulose) in a Michael addition in alkaline medium would not lose this advantage. In this reaction, a hydroxy group of the glucose reacts with a double bond of the maleic acid with formation of an ether and with conservation of the two functional carboxyl groups. In this reaction a succinic acid ether of the starch is formed (a succinyl starch, not starch succinate, the latter would be a succinic acid ester). The disadvantage in this connection is that the yields of the maleic acid are minimal (conventionally less than 10 %) and the achievable substitution rate is small. Accordingly, it is not economical and not sufficiently efficient in its effects. Additions to a double bond with glucose or other carbohydrates are generally not efficient. Moreover, the maleic acid anhydride reacts with the starch to maleic acid ester (starch maleate) in this Michael reaction under alkaline conditions, so that in this reaction also one of the two carboxyl groups is lost as an ionic group (see R. L. Davidson, "Handbook of Water-soluble Gums and Resins", Chapter 22, pp. 22-40, 1980).

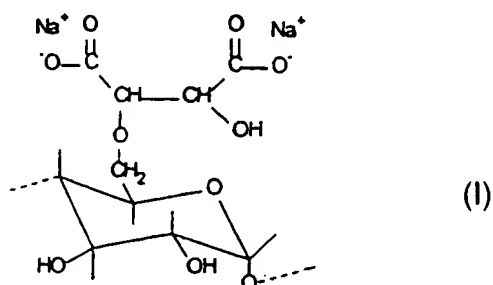
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In particular in connection with the natural base of polysaccharides there is still a high need in regard to polysaccharide derivatives with multi-functional properties. The object of the invention resides therefore in the provision of polysaccharide derivatives in which both carboxyl groups are preserved.

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Surprisingly, new malatyl polysaccharides were found which can be prepared from polysaccharides and cis-epoxy succinate or other epoxy carboxylic acids, wherein the carboxyl groups are maintained in their preparation. However, it is also possible to use the derivatives of polysaccharides instead of native polysaccharides. This

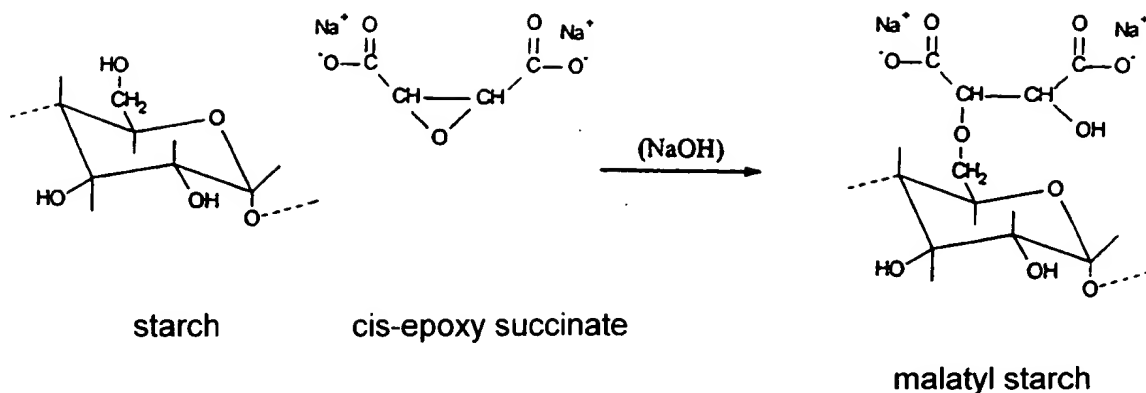
makes possible the preparation of products with multi-variable properties.

The preparation of malatyl polysaccharides can be realized with solid epoxy succinate as well as with a epoxy succinate solution. This has the advantage that it is not required to start with pure epoxy succinate but instead one can produce it in situ from other inexpensive starting materials (by a known method). For example, it is possible to produce the cis-epoxy succinate from maleic acid and hydrogen peroxide or from hydroquinone and hydrogen peroxide. The solution can be concentrated in vacuum, and the concentrated epoxy succinate solution is then added as a reagent to the starch, which is made alkaline, in an alcohol suspension or acetone suspension.

An advantageous compound according to the invention is malatyl starch, a malic acid ether of starch of the general formula (I):



The malatyl starch is obtained by the reaction of cis-epoxy succinate (disodium salt of cis-epoxy succinic acid) with starch in an alkaline suspension. The use of epoxy succinic acid itself is also possible, but in this case an equivalent amount of base must be added previously in the basification step. Schematic:



Producing epoxy succinate itself (and other epoxy carboxylic acids) is described in several publications (DE 2213260; DE 2347224; G.B. Payne, P.H. Williams, J. Org. Chem., 24, pp. 54ff, 1959; G.B. Payne, J. Org. Chem., 24, p. 2048ff, 1959; E. Weitz, H. Schobbert, H. Seibert, Chem. Ber., 68, p. 1163, 1935).

The reaction of cis-epoxy succinate or other epoxy carboxylic acids with starch, cellulose, or other polysaccharides is however unknown. Currently, no indication has been found that these substances (for example, malatyl starch) have been described in any other publication.

Also, it has been attempted to produce ionic starch derivatives or polysaccharides derivatives with other epoxy carboxylic acids. These include, inter alia, epoxy crotonic acid, epoxy cinnamic acid, epoxy acrylic acid or epoxy aconitic acid. However, for these epoxy carboxylic acids only average to low yields were obtained so that only low substitution rates will be adjustable.

In addition to the preparation of malatyl starch from starch with an epoxy succinate solution, the preparation of malatyl starch from solid epoxy succinate and basified

starch is the more elegant method because there is no possibility of introducing contaminants of the epoxy succinate preparation. However, a possible introduction of contaminants is not of great importance because the malatyl starch at the end of the preparation process is filtered from the suspension and is washed with an alcohol and water mixture.

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For obtaining improved substitution yields, it was found to be beneficial to adjust a pH value of 9-13 with sodium hydroxide in the alcohol suspension and to employ a molar ratio of NaOH to starch that is not higher than 1:1 to 2:1 but to work as much as possible with smaller ratios. Advantageous is a NaOH concentration of approximately 3-5 mol/l. The ratio depends also on which molar amount of cis-epoxy succinate is used. When a greater molar ratio of epoxy succinate/starch is selected, more NaOH must be employed for a better activation of the starch (in this connection, the limit NaOH/starch of 1/1 to 2/1 should also be observed). The yields of epoxy succinate are approximately 40-85 % so that a substitution rate of 0.2 to 0.6 is easily adjustable.

The fully neutralized malatyl starch (as a sodium salt) with a substitution ratio of 0.15 to 0.6 can be easily dissolved in cold water, the solutions are clear, and have a pH value of 7.8-8.1. The unneutralized acid form of the malatyl starch is sparingly soluble in water and has a pH value of 2.5-2.8 as a suspension of 1 %.

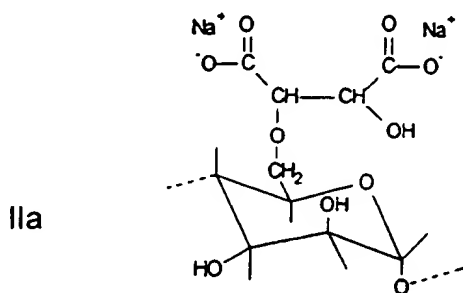
After the reaction the malatyl starch can be adjusted with hydrochloric acid, acetic acid or other acids to the desired pH value. This is performed advantageously in an alcohol suspension wherein the contents of water of the suspension medium should be a minimum of 15 % and a maximum of 30 %. The adjustment of the pH value has a great influence on the final properties of the malatyl starch. When drying the partially neutralized malatyl starch compounds, having a pH value of 3.0-7.5, an intermolecular and intramolecular cross-linking occurs which results in that

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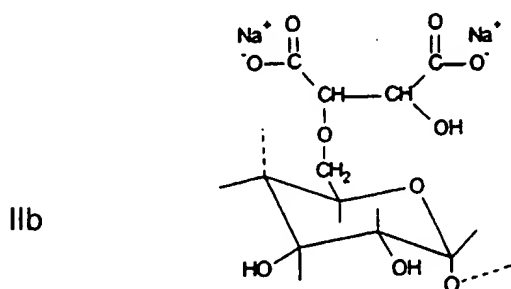
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the malatyl starch becomes insoluble in water and forms viscous to highly viscous gels. When using at the same time a di-functional or poly-functional cross-linking agent (for example, an organic dichloro compound during the reaction), it is also possible to obtain stable gel-forming products.

- 5 A further advantageous compound according to the invention is the group of malatyl galactomannans of the general formula (IIa) on the basis of mannose



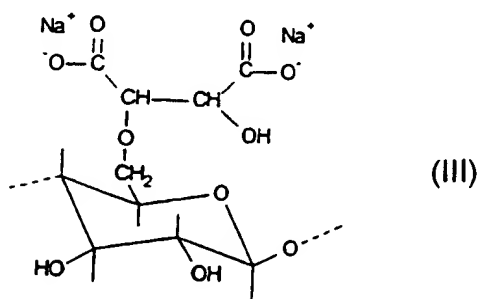
and/or the general formula (IIb) based on galactose.



- 10 In analogy to the preparation of malatyl starch, the malatyl guaran can also be produced from cis-epoxy succinate and guaran. The preparation of malatyl guaran is also carried out in suspension. It is advantageous to use methanol and isopropanol with approximately 20 % water. The basification should be carried out with sodium hydroxide at approximately 20 °C. The yields relative to cis-epoxy succinate are somewhat less than for the malatyl starch preparation. The solutions
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of malatyl guaran are more viscous than those of malatyl starch.

A further advantageous compound according to the invention is malatyl cellulose of the general formula (III)



Malatyl cellulose can be produced from cellulose and cis-epoxy succinate. Advantageously, the reaction is carried out in isopropanol with a total of approximately 20 % water and a previous basification with sodium hydroxide at approximately 15 °C. Heating during basification does not provide any advantages. The yields relative to cis-epoxy succinate are worse than for the malatyl starch preparation. The solutions of malatyl cellulose are more viscous than those of malatyl starch.

The final properties of malatyl cellulose and malatyl guaran can also be varied by adjusting the pH value before drying so that in this connection also cross linking can be adjusted.

- 15 The compounds according to the invention are suitable as a result of their properties in their un-crosslinked form, as complexing agents for polyvalent cations, for example, in detergents or for organic substances in the pharmaceutical sector. In their crosslinked form they are suitable as thickening agents because they are insoluble in water, swell strongly and form gels. Depending on the density of the
- 20 crosslinking, slightly or highly viscous gels form which can be used, for example, in

hygiene articles or in the medical field. For a very great degree of crosslinking, they can swell only minimally and can be used, for example, as ion exchangers for aqueous system or as additives in pharmaceutical applications (for example, tablet bursting agents, suspension stabilizers etc.).

5 In the following, embodiments of the invention will be explained in more detail.

Example 1

Malatyl Starch from Potato Starch and Disodium Epoxy Succinate made from Maleic Acid

Step 1A

Maleic acid reacts very quickly and completely with H_2O_2 and 2 mol-% of a catalyst in only 1.5 hours at 65 °C to disodium epoxy succinate in almost quantitative yield: maleic acid + H_2O_2 + NaOH + sodium tungstate ($Na_2WO_4 \cdot 2H_2O$).

Into a one-liter round flask with stirrer, thermometer, and dropping funnel, a solution of 116 g (1.0 mole) maleic acid in 300 ml water is introduced. To this solution a solution of 60 g (1.5 mole) NaOH in 100 ml water is added. As a result of the released neutralization heat, the temperature rises to approximately 70 °C. To the hot solution 6.6 g (0.02 mole) of sodium tungstate are added.

A pH electrode is immersed into the solution and 1.2 mole of a 30-% H_2O_2 (123 ml or 136 g; for 35-% H_2O_2 it is 103 ml or 117 g) are added. The exothermic reaction is maintained for 15 minutes with a water bath at 65 °C, and the pH value drops from approximately 5.5 to 4. With dropwise addition of a solution of 0.5 mole (20 g) NaOH in 100 ml water the reaction solution is then maintained at a minimum of pH 4. After 1-1.5 hours of stirring at approximately 65 °C, the solution is cooled to

40 °C, and the rest of the last NaOH solution is added.

The solution is concentrated at 30-40 °C in vacuum to approximately 300 ml.

Step 1B

190 g (1.0 mole) potato starch (moisture contents 15 %) are suspended in 500 ml ethanol in a four-neck glass flask provided with a stirrer, thermometer, and dropping funnel. 80 g of a 50 % by weight sodium hydroxide solution is added to the suspension under stirring within 5 minutes. The mixture is stirred for 30 minutes at a temperature of 20-25 °C. Subsequently, 150 ml of the concentrated epoxy succinate solution of step 1A is added to the flask at 25 °C. The reaction mixture is then heated within 30 minutes to 70 °C and is stirred for 4 hours at this temperature. After cooling to 20-25 °C, the suspension is filtered and the residue is washed twice with 80 % methanol and with pure methanol. The malatyl starch is then dried at 110 °C in a circulating air drying chamber to a residual moisture of approximately 5-10 %. A substitution rate DS = 0.35 is achieved (titration of the acidic form). In the following, this malatyl starch is identified with MS/W or MS35/W.

Example 2

Malatyl Starch from Potato Starch and Disodium Epoxy Succinate
made from Hydroquinone

Step 2A

Disodium epoxy succinate from: hydroquinone + H₂O₂ + NaOH

The oxidation of hydroquinone by alkali and H₂O₂ takes place - via the quinone - as

that of the quinone itself. For preparative purposes, it is therefore simpler to employ hydroquinone. The reaction takes place with great heat development and is finally very vigorous. However, with a suitable selection of the reaction conditions and flasks cooling is not required.

5 In a 5-l beaker with magnetic stirrer, 110 g (1 mole) hydroquinone together with 690 ml 35-% (8 mole) H_2O_2 is heated under stirring to 70-80 °C (there is hardly any gas development to be observed) and then a NaOH solution (of 120 g NaOH and 500 ml water) is added so fast or so slow via a dropping funnel that the vigorous reaction will not become too violent. The mixture turns a dark reddish brown upon adding the NaOH and additional heat is developed. Approximately 5 minutes after completed NaOH addition, the reaction is completed, and the solution is colorless. The solution is then concentrated at 30-40 °C in vacuum to 200-300 ml.

Step 2B

10 190 g (1.0 mole) potato starch (moisture contents 15 %) are suspended in 500 ml ethanol in a four-neck glass flask provided with a stirrer, thermometer, and dropping funnel. 80 g of a 50 % by weight sodium hydroxide solution is added to the suspension under stirring within 5 minutes. The mixture is stirred for 30 minutes at a temperature of 20-25 °C. Subsequently, 150 ml of the concentrated epoxy succinate solution of step 2A is added to the flask at 25 °C. The reaction mixture is then heated within 30 minutes to 70 °C and is stirred for 4 hours at this temperature. After cooling to 20-25 °C, the suspension is filtered and the residue is washed twice with 80 % methanol and with pure methanol. The malatyl starch is then dried at 110 °C in a circulating air drying chamber to a residual moisture of approximately 5-10 %. A substitution rate $\text{DS} = 0.15$ is achieved (titration of the acidic form). In the following, this malatyl starch is identified with MS/H or MS15/W.

Example 3

Malatyl Starch from Potato Starch and Disodium Epoxy Succinate

Step 3A

Preparation of disodium epoxy succinate, as described in step 1A. Isolation:

- 5 The solution is concentrated at 30-40 °C in vacuum to 300 ml and is introduced with stirring into 1.5 liter acetone to thereby precipitate 160 g of colorless disodium epoxy succinate. The precipitated product is filtered and washed with acetone.

Step 3B

- 10 190 g (1.0 mole) potato starch (moisture contents 15 %) are suspended in 400 ml ethanol in a four-neck glass flask provided with a stirrer, thermometer, and dropping funnel. 80 g of a 50 % by weight sodium hydroxide solution is added to the suspension under stirring within 5 minutes. The mixture is stirred for 30 minutes at a temperature of 20-25 °C. Subsequently, 150 g (0.85 mole) solid disodium epoxy succinate of step 3A is added in portions to the flask at 25 °C. The reaction mixture is then heated within 30 minutes to 50 °C and is stirred for 4 hours at this temperature. After cooling the suspension to 20 °C, it is neutralized with acetic acid (99 %) to a pH of 8-9, then filtered and the residue is washed twice with 80 % methanol and with pure methanol. The malatyl starch is then dried at 110 °C in a circulating air drying chamber to a residual moisture of approximately 5-10 %. A substitution ratio DS = 0.5 is achieved (titration of the acid form). In the following, this malatyl starch is identified with MS05.
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Example 4

Malatyl Guaran from Guar Flour and Disodium Epoxy Succinate

42 g (0.26 mole) guar flour (moisture contents 9 %) are suspended in 400 ml isopropanol and 60 ml water in a four-neck glass flask provided with stirrer, thermometer and dropping funnel. 20 g of a 50 % by weight NaOH solution is added under stirring to the suspension. The mixture is then stirred for 30 minutes at a temperature of 20 °C. Subsequently, 31 g (0.176 mole) solid disodium epoxy succinate of step 3A is added to the flask in portions at 25 °C. The reaction mixture is then heated within 30 minutes to 60 °C, is stirred for 4 hours at this temperature, and allowed to stand over night. The cooled suspension is neutralized with acetic acid (99 %) to a pH of 8-9, then filtered and the residue is washed twice with 80 % methanol and with pure methanol. The malatyl guaran is then dried at 110 °C in a circulating air drying chamber to a residual moisture of approximately 5-10 %. A substitution ratio DS = 0.4 is achieved (titration of the acid form).

Example 5

Malatyl Cellulose from Fir Cellulose Powder and Disodium Epoxy Succinate

41 g (0.25 mold) cellulose (moisture contents 4 %) are suspended in 400 ml isopropanol and 80 ml water in a four-neck glass flask provided with stirrer, thermometer and dropping funnel. 10 g NaOH (scales) are added under stirring to the suspension. The mixture is stirred for 60 minutes at a temperature of approximately 15 °C. Subsequently, 53 g (0.3 mole) solid disodium epoxy succinate (see step 3A) is added to the flask in portions at 25 °C. The reaction mixture is then heated within 30 minutes to 70 °C and stirred for 4 hours at this temperature. After cooling the suspension to 20-25 °C, it is neutralized with acetic acid (99 %) to a pH of 8-9, then filtered and the residue is washed twice with 80 % methanol and with pure methanol. The malatyl cellulose is then dried at 110 °C in a circulating air drying chamber to a residual moisture of approximately 5-10 %. A substitution ratio DS = 0.6 is achieved (titration of the acid form).

The structural examinations by means of infrared spectroscopy (FT-IR) and nuclear magnetic resonance spectroscopy (^{13}C -NMR) show that these are starch derivatives which contain unequivocally carboxyl groups (see in this connection Figs. 1 through 4 for FT-IR and Figs. 5 and 6 for ^{13}C -NMR as well as comparative Tables 1 and 2).

The typical starch bands show at 1021 to 1236 cm^{-1} and the bands for the carboxyl group can be seen clearly at 1609 and 1607 cm^{-1} (-COO) and at 1703 and 1706 (-COOH). No ester bands at 1760 cm^{-1} are present. The resonance peaks of carbon of the carboxyl group can be identified at 178.2 and 176.5 ppm. Resonance peaks of the ester at approximately 160 ppm are also not present here so that the presence of an ether can be assumed.

Examinations by means of gel permeation chromatography (GPC) show unequivocally that the desired high molecular substances are present (see in this connection Figs. 7 and 8 for MS15/H and Figs. 9 and 10 for MS35/W). The molecular weights are approximately 2 to 8 million g/mole. A 1 % solution has an average viscosity of 500-1000 mPa.s (depending on the substitution rate).

Table 1: Comparison of the Bands (cm^{-1}) of the FT-IR Spectra (Figs. 1 and 2)

MS35/W	MS15/H	potato starch
530	529	525
576	577	580
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708	709	710
762	763	762
848	850	855
931	931	931

1021	1022	1022
1082	1082	1081
1156	1156	1158
1236	1236	1236
1391	1370	1364
1607	1609	--
--	--	1650
1706	1703	--

Table 2: Comparison of Resonance Peaks (ppm) of ^{13}C -NMR Spectra (Figs. 5 and 6)

MS15/H	MS35/H
61.2	61.2
70.1	
71.8	71.8
72.1	72.1
73.8	73.8
77.8	77.8
80.0	
81.6	
82.5	83.8
100.1	100.1
176.5	178.2

The malatyl derivatives are stable and can be stored without problems so that no

structural or property changes will result (average storage at 25±3 °C and 60±5 % humidity).

Example 6 Use as Complexing Agent

5 The assay was carried out according to the calcium carbonate method. For this purpose, 1 g of malatyl starch was dissolved in 100 ml distilled water, 10 ml of a 2 % sodium carbonate solution was added, and then calcium acetate mono hydrate solution (with 44.1 g/l) was used for titration up to permanent turbidity.

Table 3: Complexing Results

substance	DS	mg/g
malatyl starch MS/H	0.15	110
malatyl starch MS/W	0.35	225
malatyl starch MS05	0.5	320
succinic acid, disodium (comparison)		250
penta-sodium triphosphate (comparison)		200

According to this method, the complexing behavior of the substance malatyl starch according to the invention is better than that of pure succinic acid and that of pentasodium triphosphate, relative to the employed amount (in mg/g). Moreover, it was found that the formed turbidity (CaCO_3) did not precipitate immediately but sedimentation of the turbidity took several hours when using malatyl starch and occurred only after days when using MS/H.